AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings of claims in the application:

Claim 1 (currently amended): A method comprising topically applying a liquid formulation to a surface of a mammal the liquid formulation comprising between about [[6]] 10% (w/v) to about [[60]] 30% (w/v) of a TRPV1 agonist, at least a first penetration enhancer and a second penetration enhancer, wherein the first penetration enhancer is propylene glycol or diethylene glycol monoethyl ether and the second penetration ~~enhancers are different and are~~ enhancer is selected from the group consisting of ~~propylene glycol, diethylene glycol monoethyl ether,~~ ethyl oleate, oleic acid, oleyl alcohol, benzyl alcohol and menthone, and optional additional components comprising not more than 5% (w/v) of the liquid formulation, and wherein a single application of the liquid formulation results in pain relief for at least two weeks.

Claim 2-6 (cancelled)

Claim 7 (previously presented): The method of claim 1 wherein the TRPV1 agonist is capsaicin.

Claim 8 (cancelled)

Claim 9 (previously presented): The method of claim 1 wherein the mammal is a human.

Claim 10 (original): The method of claim 9 wherein the human suffers from a capsaicin-responsive condition.

Claim 11 (previously presented): The method of claim 1 wherein 2 to 7 days after topically applying the liquid formulation to the surface of a mammal, the density of functional nociceptive nerve fibers in the epidermis and dermis of the mammal is decreased by at least about 20%.

Claim 12-13 (cancelled)

Claim 14 (withdrawn): A method of reducing the density of functional nociceptive nerve fibers in a selected region of a subject, comprising contacting the region with an immediate-release composition that contains a TRPV1 agonist and one or more penetration enhancers, wherein said composition delivers at least about 3 nmoles agonist to skin as measured in a mouse skin absorption assay.

Claim 15 (withdrawn): A method of reducing the density of functional nociceptive nerve fibers in a selected region of a subject, comprising contacting the region with a composition that contains a TRPV1 agonist and a solvent system comprising one or more penetration enhancers, wherein said composition delivers at least about 3 nmoles agonist to skin as measured in a mouse skin absorption assay, and wherein at least about 5 μl composition is delivered to each cm^2 of the region in about 15 minutes.

Claim 16 (withdrawn): The method of claim 14 wherein the selected region is on the surface of skin or mucosa.

Claim 17 (withdrawn): The method of claim 14 wherein said composition delivers at least about 6 nmoles agonist to skin.

Claim 18 (withdrawn): The method of claim 17 wherein said composition delivers at least about 16 nmoles to skin.

Claim 19 (withdrawn): The method of claim 18 wherein said composition delivers at least about 32 nmoles to skin.

Claim 20 (withdrawn): The method of claim 19 wherein said composition delivers at least about 49 nmoles to skin.

Claim 21 (withdrawn): The method of claim 20 wherein said composition delivers at least about 65 nmoles agonist to skin.

Claim 22 (withdrawn): The method of claim 21 wherein said composition delivers from about 5 nmoles to about 290 nmoles agonist to skin.

Claim 23 (withdrawn): The method of claim 14 wherein the depot effect of said contacting is less than about 0.25 as measured in a mouse skin absorption assay.

Claim 24 (withdrawn): The method of claim 23 wherein the depot effect is less than about 0.1.

Claim 25 (withdrawn): The method of claim 24 wherein the depot effect is less than about 0.02.

Claim 26 (withdrawn): The method of claim 25 wherein the depot effect is less than about 0.001.

Claim 27 (withdrawn): The method of claim 14 wherein the depot effect is in a range of about 0.001 to about 0.25.

Claim 28 (withdrawn): The method of claim 14 wherein the distribution effect of said contacting is in the range of 0.5 to 2, as measured in a mouse skin absorption assay.

Claim 29 (withdrawn): The method of claim 14 wherein the composition comprises the TRPV1 agonist and a solvent system, wherein penetration enhancer(s) make up at least 20% (v/v) of the solvent system.

Claim 30 (withdrawn): The method of claim 29 wherein penetration enhancer(s) make up at least 50% (v/v) of the solvent system.

Claim 31 (withdrawn): The method of claim 30 wherein penetration enhancer(s) make up at least 90% (v/v) of the solvent system.

Claim 32 (withdrawn): The method of claim 31 wherein penetration enhancer(s) make up at least 95% (v/v) of the solvent system.

Claim 33 (withdrawn): The method of claim 14 wherein the solvent system comprises a penetration enhancer selected from the group consisting of ethers, esters, alcohols, fatty acids, fatty acid esters, fatty alcohols, polyols, terpenes, and amines.

Claim 34 (withdrawn): The method of claim 14 wherein the solvent system comprises a penetration enhancer selected from the group consisting of fatty alcohols and terpenes.

Claim 35 (withdrawn): The method of claim 14 wherein said solvent system comprises a penetration enhancer selected from the group consisting of l-menthone, dimethyl isosorbide, caprylic alcohol, lauryl alcohol, oleyl alcohol, ethylene glycol, diethylene glycol, triethylene glycol, butylene glycol, valeric acid, pelargonic acid, caproic acid, caprylic acid, lauric acid, oleic acid, isovaleric acid, isopropyl butyrate, isopropyl hexanoate, butyl acetate, methyl acetate, methyl valerate, ethyl oleate, poloxamer, d-piperitone, methylnonenoic acid, methylnonenoic alcohol, and d-pulegone.

Claim 36 (withdrawn): The method of claim 14 wherein said composition comprises said TRPV1 agonist at a concentration of from 0.05% (w/v) to 60% (w/v).

Claim 37 (withdrawn): The method of claim 36 wherein the TRPV1 agonist is a vanilloid.

Claim 38 (withdrawn): The method of claim 37 wherein the TRPV1 agonist is capsaicin.

Claim 39 (withdrawn): The method of claim 36 wherein said composition comprises said TRPV1 agonist at a concentration of from 1% (w/v) to 20% (w/v).

Claim 40 (withdrawn): The method of claim 14 wherein the subject is a human.

Claim 41 (withdrawn): The method of claim 14 wherein said contacting is by topical application or instillation.

Claim 42 (withdrawn): The method of claim 14 wherein a 15 minute application of the composition to skin of a mammal results in a decrease in the density of functional nociceptive nerve fibers by at least about 50%, wherein the mammal is selected from the group consisting of a mouse or a human.

Claim 43 (withdrawn): The method of claim 14 wherein the subject is a human.

Claim 44 (withdrawn): The method of claim 43 wherein the subject suffers from a capsaicin-responsive condition.

Claim 45 (withdrawn): The method of claim 44 wherein the capsaicin-responsive condition is neuropathic pain, pain produced by mixed nociceptive and neuropathic etiologies, inflammatory hyperalgesia, vulvodynia, interstitial cystitis, overactive bladder, prostatic hyperplasia, rhinitis, rectal hypersensitivity, burning mouth syndrome, oral mucositis, herpes, prostatic hypertrophy, dermatitis, pruritis, itch, tinnitus, psoriasis, warts, skin cancers, headaches, or wrinkles.

Claim 46 (withdrawn): A method of treating a capsaicin-responsive condition in a subject, comprising non-occlusive or non-adherent administration of a composition that contains a TRPV1 agonist and at least one penetration enhancer, wherein said composition delivers at least about 3 nmoles agonist to skin as measured in a mouse skin absorption assay.

Claim 47 (withdrawn): A method of treating a capsaicin-responsive condition in a subject, comprising administration of a composition that contains a TRPV1 agonist and at least two penetration enhancers, wherein said composition delivers at least about 3 nmoles agonist to skin as measured in a mouse skin absorption assay.

Claim 48 (withdrawn): The method of claim 46 wherein the composition is applied to an area on the surface of skin, mucosa, or endothelium.

Claim 49 (withdrawn): The method of claim 46 wherein said composition delivers at least about 6 nmoles agonist to skin.

Claim 50 (withdrawn): The method of claim 49 wherein said composition delivers at least about 16 nmoles to skin.

Claim 51 (withdrawn): The method of claim 50 wherein said composition delivers at least about 32 nmoles to skin.

Claim 52 (withdrawn): The method of claim 51 wherein said composition delivers at least about 49 nmoles to skin.

Claim 53 (withdrawn): The method of claim 52 wherein said composition delivers at least about 65 nmoles agonist to skin.

Claim 54 (withdrawn): The method of claim 53 wherein said composition delivers from about 5 nmoles to about 290 nmoles agonist to skin.

Claim 55 (withdrawn): The method of claim 46 wherein the depot effect of said contacting is less than about 0.25 as measured in a mouse skin absorption assay.

Claim 56 (withdrawn): The method of claim 55 wherein the depot effect is less than about 0.1.

Claim 57 (withdrawn): The method of claim 56 wherein the depot effect is less than about 0.02.

Claim 58 (withdrawn): The method of claim 57 wherein the depot effect is less than about 0.001.

Claim 59 (withdrawn): The method of claim 55 wherein the depot effect is in a range of about 0.001 to about 0.25.

Claim 60 (withdrawn): The method of claim 46 wherein the distribution effect of said contacting is in the range of 0.5 to 2 as measured in a mouse skin absorption assay.

Claim 61 (withdrawn): The method of claim 46 wherein the composition comprises the TRPV1 agonist and a solvent system, wherein penetration enhancer(s) make up at least 20% (v/v) of the solvent system.

Claim 62 (withdrawn): The method of claim 61 wherein penetration enhancer(s) make up at least 50% (v/v) of the solvent system.

Claim 63 (withdrawn): The method of claim 62 wherein penetration enhancer(s) make up at least 90% (v/v) of the solvent system.

Claim 64 (withdrawn): The method of claim 63 wherein penetration enhancer(s) make up at least 95% (v/v) of the solvent system.

Claim 65 (withdrawn): The method of claim 46 wherein the solvent system comprises a penetration enhancer selected from the group consisting of ethers, esters, alcohols, fatty acids, fatty acid esters, fatty alcohols, polyols, terpenes, and amines.

Claim 66 (withdrawn): The method of claim 65 wherein the solvent system comprises a penetration enhancer selected from the group consisting of fatty alcohols and terpenes.

Claim 67 (withdrawn): The method of claim 66 wherein said solvent system comprises a penetration enhancer selected from the group consisting of l-menthone, dimethyl isosorbide, caprylic alcohol, lauryl alcohol, oleyl alcohol, ethylene glycol, diethylene glycol, triethylene glycol, butylene glycol, valeric acid, pelargonic acid, caproic acid, caprylic acid, lauric acid, oleic acid, isovaleric acid, isopropyl butyrate, isopropyl hexanoate, butyl acetate, methyl acetate, methyl valerate, ethyl oleate, poloxamer, d-piperitone, methylnonenoic acid, methylnonenoic alcohol, and d-pulegone.

Claim 68 (withdrawn): The method of claim 46 wherein said composition comprises said TRPV1 agonist at a concentration of from 0.05% (w/v) to 60% (w/v).

Claim 69 (withdrawn): The method of claim 68 wherein the TRPV1 agonist is a vanilloid.

Claim 70 (withdrawn): The method of claim 69 wherein the TRPV1 agonist is capsaicin.

Claim 71 (withdrawn): The method of claim 70 wherein said composition comprises said TRPV1 agonist at a concentration of from 1% (w/v) to 20% (w/v).

Claim 72 (withdrawn): The method of claim 71 wherein a 15 minute application of the composition to skin of a mammal results in a decrease in the density of functional nociceptive nerve fibers by at least about 20% when measured 2 to 7 days after said contacting step.

Claim 73 (withdrawn): The method of claim 72 wherein a 15 minute application of the composition to skin of a mammal results in a decrease in the density of functional nociceptive nerve fibers by at least about 50% when measured 7 days after said contacting step.

Claim 74 (withdrawn): The method of claim 14 wherein the density of functional nociceptive nerve fibers in the epidermis and dermis underlying said region is decreased by at least about 20% when measured 7 days after said contacting step.

Claim 75 (withdrawn): The method of claim 46 wherein the composition is administered topically.

Claim 76 (withdrawn): The method of claim 75 wherein the composition is administered by instillation.

Claim 77 (withdrawn): The method of claim 46 wherein the composition is administered by injection.

Claim 78 (withdrawn): The method of claim 46 wherein the composition is administered in the form of a microemulsion.

Claim 79 (withdrawn): The method of claim 46 wherein the capsaicin-responsive condition is neuropathic pain, pain produced by mixed nociceptive and neuropathic etiologies, inflammatory hyperalgesia, vulvodynia, interstitial cystitis, overactive bladder, prostatic hyperplasia, rhinitis, rectal hypersensitivity, burning mouth syndrome, oral mucositis, herpes, prostatic hypertrophy, dermatitis, pruritis, itch, tinnitus, psoriasis, warts, skin cancers, headaches, or wrinkles.

Claim 80 (withdrawn): The method of claim 79 wherein the neuropathic pain is associated with diabetic neuropathy, postherpetic neuralgia, HIV/AIDS, traumatic injury, complex regional pain syndrome, trigeminal neuralgia, erythromelalgia and phantom pain.

Claim 81 (withdrawn): The method claim 80 wherein one or two applications of the composition provide persistent relief.

Claim 82 (withdrawn): The method claim 81 wherein one application of the composition provides persistent relief.

Claim 83 (withdrawn): The method of claim 46 wherein the composition is administered to an area on the surface of the skin and subsequent to administration the area is cleaned to remove any residual agonist.

Claim 84 (withdrawn): The method of claim 83 wherein the area is cleaned using a composition containing at least 60% (w/w/) polyethylene glycol.

Claim 85 (currently amended): A liquid formulation comprising:

between about [[6]] 10% (w/v) to about [[60]] 30% (w/v) of a TRPV1 agonist,

at least a first penetration enhancer and a second penetration enhancer, wherein the first penetration enhancer is propylene glycol or diethylene glycol monoethyl ether and the second penetration ~~enhancers are different and are~~ enhancer is selected from the group consisting of ~~propylene glycol, diethylene glycol monoethyl ether,~~ ethyl oleate, oleic acid, oleyl alcohol, benzyl alcohol and menthone [[,]]; and

optional additional components comprising not more than 5% (w/v) of the liquid formulation.

Claim 86 (currently amended): A liquid formulation comprising:

between about [[6]] 10% (w/v) to about [[60]] 30% (w/v) of capsaicin;

at least a first penetration enhancer and a second penetration enhancer, wherein the first penetration enhancer is propylene glycol or diethylene glycol monoethyl ether and the second penetration ~~enhancers are different and are~~ enhancer is selected from the group consisting of ~~propylene glycol, diethylene glycol monoethyl ether,~~ ethyl oleate, oleic acid, oleyl alcohol, benzyl alcohol, and menthone; and

optional additional components comprising not more than 5% (w/v) of the liquid formulation.

Claim 87 (cancelled)

Claim 88 (previously presented): The liquid formulation of claim 85 wherein said first and second penetration enhancers, taken together, comprise at least 50% (v/v) of the liquid formulation.

Claim 89 (previously presented): The liquid formulation of claim 88 wherein said first and second penetration enhancers, taken together, comprise at least 75% (v/v) of the liquid formulation.

Claim 90 (currently amended): The liquid formulation of claim 89 wherein said first and second penetration enhancers, taken together, comprise at least [[95]] 90% (v/v) of the liquid formulation.

Claim 91-92 (cancelled)

Claim 93 (previously presented): The liquid formulation of claim 85 wherein the TRPV1 agonist is capsaicin.

Claim 94 (cancelled)

Claim 95 (previously presented): The liquid formulation of claim 85 further comprising a local anesthetic.

Claim 96 (withdrawn): A method of treating a capsaicin-responsive condition in a subject comprising administering a composition of claim 85.

Claim 97 (previously presented): The liquid formulation of claim 85 wherein the liquid formulation is contained in a microemulsion.

Claim 98 (previously presented): A system for treating a capsaicin-responsive condition, the system comprising the liquid formulation of claim 85 and a non-occlusive and/or non-adherent applicator device for applying the liquid formulation.

Claim 99 (previously presented): The system of claim 98 wherein the applicator device is pre-filled with the liquid formulation.

Claim 100 (previously presented): The system of claim 98 wherein the liquid formulation is contained in a container separate from the device.

Claim 101 (previously presented): The system of claim 98 further comprising measuring marks on the applicator device for assisting a user in determining the amount of the liquid formulation in the applicator device.

Claim 102 (original): The system of claim 98 wherein the applicator device is a metered dose aerosol, a stored-energy metered dose pump or a manual metered dose pump.

Claim 103 (original): The system of claim 98 wherein the applicator device is a sponge, brush, or swab.

Claim 104 (original): A kit comprising the system of claim 98 and a cleaning composition for removal of residual agonist.

Claim 105 (original): The kit of claim 104 wherein the cleaning composition comprises at least about 60% polyethylene glycol.

Claim 106 (cancelled)

Claim 107 (withdrawn): A method of treating a patient suffering from a capsaicin-responsive condition that affects a body part, comprising immersing the body part within the microemulsion claim 106.

Claim 108 (withdrawn): The method of claim 107 wherein the affected area of tissue is immersed within the microemulsion for a predetermined length of time.

Claim 109 (withdrawn): A method of providing a therapeutic bath comprising adding the TRPV1 agonist microemulsion of claim 106 to a basin.

Claim 110 (previously presented): A therapeutic bath apparatus comprising a basin capable of receiving an affected area of tissue therein, wherein the basin has a bottom surface and a wall structure extending upwardly therefrom, and wherein the basin contains a fluid comprising the TRPV1 agonist microemulsion of claim 97.

Claim 111 (withdrawn): A method of reducing the density of functional nociceptive nerve fibers in a selected region of a subject, comprising contacting the region with the TRPV1 agonist microemulsion of claim 106.

Claim 112 (withdrawn): The method of claim 111 wherein the selected region is bladder endothelium.

Claim 113 (withdrawn): A method of treating a capsaicin-responsive condition in a subject comprising administration of a TRPV1 agonist microemulsion of claim 106.

Claim 114 (withdrawn): The method of claim 21 wherein the capsaicin-responsive condition is overactive bladder and the TRPV1 agonist microemulsion is instilled into the bladder.

Claim 115 (withdrawn): A method for identifying a composition as useful for therapeutic delivery of a TRPV1 agonist to a subject comprising determining the depot effect for a solution consisting of the composition and the TRPV1 agonist, where a depot effect less than 0.2 indicates the composition is useful for therapeutic delivery of a TRPV1 agonist.

Claim 116 (withdrawn): The method of claim 115 further comprising determining the amount of agonist delivered to skin epidermis and dermis after a specified time when the composition is applied to the skin surface.

Claim 117 (withdrawn): A method for ranking two or more compositions according to their utility for therapeutic delivery of a TRPV1 agonist to a subject comprising determining for each composition the depot effect for a solution consisting of the composition and the TRPV1 agonist or a different TRPV1 agonist, comparing the values obtained for each composition, and ranking them compositions according to the values, where a composition with a lower value is ranked more suitable for therapeutic delivery of the TRPV1 agonist. In one embodiment, there is a further step of determining, for each composition, the amount

Claim 118 (cancelled)

Claim 119 (withdrawn): A method of increasing the amount of a molecule applied to a skin or mucosal surface that enters the underlying epidermal and dermal layers by applying the molecule in a composition comprising methylnonenoyl alcohol or methylnonenoic acid.

Claim 120 (withdrawn): The method of claim 119 wherein the molecule is a therapeutically active agent.

Claim 121(withdrawn): The method of claim 120 wherein the molecule is a TRPV1 agonist.

Claim 122-126 (cancelled)

Claim 127 (currently amended): The method of claim [[123]] 1 wherein the liquid formulation comprises between about 10% (w/v) to about 20% (w/v) of the TRPV1 agonist.

Claim 128 (cancelled)

Claim 129 (previously presented): The method of claim 1 wherein the liquid formulation comprises about 10% (w/v) of the TRPV1 agonist.

Claim 130 (previously presented): The method of claim 1 wherein a single application of the liquid formulation results in pain relief for at least one month.

Claim 131 (previously presented): The method of claim 130 wherein the single application of the liquid formulation results in pain relief for at least three months.

Claim 132 (previously presented): The method of claim 131 wherein the single application of the liquid formulation results in pain relief for at least six months.

Claim 133 (previously presented): The method of claim 1 wherein a single application of the liquid formulation results in neuropathic pain relief.

Claim 134-135 (cancelled)

Claim 136 (currently amended): The liquid formulation of claim [[135]] 85 wherein the liquid formulation comprises between about 6% (w/v) to about 20% (w/v) of the TRPV1 agonist.

Claim 137-140 (cancelled)

Claim 141 (previously presented): The liquid formulation of claim 85 comprising about 10% (w/v) of the TRPV1 agonist.

Claim 142 (previously presented): The liquid formulation of claim 85 wherein a single application of the liquid formulation results in pain relief for at least one month.

Claim 143 (previously presented): The liquid formulation of claim 142 wherein the single application of the liquid formulation results in pain relief for at least three months.

Claim 144 (previously presented): The liquid formulation of claim 143 wherein the single application of the liquid formulation results in pain relief for up to about six months.

Claim 145 (previously presented): The liquid formulation of claim 85 wherein a single application of the liquid formulation results in neuropathic pain relief.